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Effect of sustained experimental muscle pain on joint position sense

Simon J. Summers^{a,*}, Siobhan M. Schabrun^b, Rogerio P. Hirata^c, Thomas Graven-Nielsen^d, Rocco Cavaleri^a, Lucy S. Chipchase^{a,e}

Abstract

Introduction: Joint position sense (JPS) is impaired in clinical musculoskeletal pain conditions, but when this impairment develops in the transition from initial to prolonged pain is not known.

Objectives: This study assessed whether progressively developing sustained experimentally induced muscle pain impacts JPS in healthy individuals.

Methods: Twenty-eight healthy individuals received injection of nerve growth factor (NGF) into the right extensor carpi radialis brevis muscle on days 0 and 2 to induce sustained pain and hyperalgesia. Wrist JPS was assessed 2 days before day 0 (day -2), before the injection on days 0 and 2, and on days 4 and 14. Joint position sense was quantified as the ability to return the wrist to a neutral position following movements in the direction of radial and ulnar deviation. A 3-dimensional motion analysis system was used to calculate absolute, relative, and joint-angle repositioning errors. Numerical rating scale scores of pain intensity, body chart pain drawings, and pressure pain thresholds (PPTs) were recorded on each day.

Results: Compared with baseline, pressure pain thresholds decreased while pain intensity and area increased at day 2 ($P < 0.001$) and day 4 ($P < 0.001$) before returning to baseline on day 14 ($P > 0.13$). Relative to day 0, there was no change in wrist JPS at day 2, 4, and 14 following movements in either target direction ($P > 0.05$).

Conclusion: Despite the presence of sustained muscle pain and hyperalgesia for 4 days at the elbow, no statistical change in wrist joint position error was observed. These findings suggest that pain and hyperalgesia lasting as long as 4 days does not impair JPS.

Keywords: Joint position sense, Experimental pain, Nerve growth factor, Proprioception, Musculoskeletal pain

1. Introduction

The ability to sense the position of limb segments in space is a highly specialised proprioceptive function fundamental for movement control.³⁹ Impaired joint position sense (JPS) has been documented in a range of persistent musculoskeletal pain

conditions in the lower limb,^{7,26} cervical,^{13,15,46} and lumbar spine^{5,32,43,50} and has been associated with functional disability and fear-avoidance.³² Indeed, poor proprioception through impaired JPS has been hypothesised to result in compromised motor control that could increase the risk of injury/reoccurrence of pain.^{40,56} However, exactly when these impairments in position sense develop in the transition to sustained musculoskeletal pain is not well understood. This information is essential to understand why some people develop persistent pain while others do not and to facilitate the delivery of treatment at meaningful time-points.

Studies investigating the impact of pain on JPS using experimentally induced pain models have elicited short-lasting pain after intramuscular injection of hypertonic saline or delayed-onset muscle soreness (DOMS).^{6,17,29,44,53,54} Findings from these studies are conflicting. For instance, studies using hypertonic saline demonstrate that pain lasting between 7 and 15 minutes has no effect on JPS.^{6,17,29,44} However, in the presence of DOMS, where pain progressively develops and peaks 48 hours after eccentric exercise, impairments in JPS have been documented immediately after, 24 hours, and up to 72 hours after exercise.^{11,34,35,41,51} While exercise-induced muscle damage with eccentric exercise may underlie the reason for differences between DOMS and pain induced by hypertonic saline, current data suggest that duration of pain may impact on JPS.^{11,35} However, JPS in the transition to sustained pain over

Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article.

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days/weeks, in the absence of exercise-induced muscle damage, has not been characterised. This is relevant because pain in the absence of tissue damage is believed to be more reflective of persistent pain in clinical populations, where symptoms may exist despite no observable pathological changes to tissues.¹⁴

Pain induced by intramuscular injection of nerve growth factor (NGF) provides a clinically relevant experimental model to study the effect of prolonged pain on JPS. Unlike DOMS, where pain is sustained for up to 3 days with concurrent muscle damage,³⁸ repeated intramuscular injections of NGF have been demonstrated to elicit muscle pain and hyperalgesia for up to 14 days, with no signs of muscle damage.^{12,22–24} In addition, intramuscular injection of NGF has been shown to induce peripheral and central sensitisation that has been hypothesised to resemble the time-course and processes involved in the transition to persistent musculoskeletal pain.²¹ Thus, this study used the NGF model to investigate the effect of progressively developing, sustained muscle pain on JPS in healthy individuals. Based on studies using the DOMS pain model that show deficits in JPS in the presence of pain lasting up to 3 days,^{11,34,35,41,51} it was hypothesised that a similar duration of pain (up to 4 days), in the absence of exercise-induced muscle damage, would produce similar deficits. Specifically, we hypothesised that joint repositioning errors would be larger, indicating impaired JPS, after 4 days of sustained pain compared with errors recorded in a pain-free state at baseline.

2. Methods

2.1. Participants

Twenty-eight healthy individuals (age, mean \pm SD 23 ± 4 years; 13 females) participated. All participants were right-handed, verified by the Edinburgh Handedness Inventory.³³ Participants had no history of neurological or upper limb conditions. All participants provided written, informed consent in accordance with the Declaration of Helsinki. The institutional Human Research Ethics Committee approved the study (H11949). Other data collected as part of the protocol will be reported elsewhere including the assessment of motor variability and corticomotor excitability.

2.2. Experimental protocol

Each participant attended the laboratory on 5 occasions: day -2 , 0, 2, 4, and 14 (Fig. 1). Nerve growth factor was injected into the muscle belly of the right extensor carpi radialis brevis (ECRB) muscle on days 0 and 2. At the beginning of each session, wrist JPS was measured using a 3-dimensional motion analysis system. To assess NGF-induced pain and mechanical hyperalgesia, numerical rating scale (NRS) scores of pain intensity, body chart pain drawings, descriptors of pain using the short-form McGill pain questionnaire, and pressure pain thresholds (PPTs) were recorded on each day. The day -2 (2 days before day 0) testing session was included to assess test-retest reliability of the wrist JPS procedure in the absence of pain (day -2 vs day 0).

2.3. Sustained pain model

After cleaning the skin with alcohol, a single bolus (5 μ g, 0.2 mL) of sterile recombinant human NGF (Lonza Australia Pty Ltd, Mount Waverley, Victoria, Australia) was injected into the muscle belly of ECRB using a 1-mL syringe with a disposable needle (27 G).^{9,21,48} Injection of NGF into ECRB was chosen because this is an established model for producing sustained lateral elbow pain.^{9,12,42} The site of injection was determined by identifying a position 1 cm

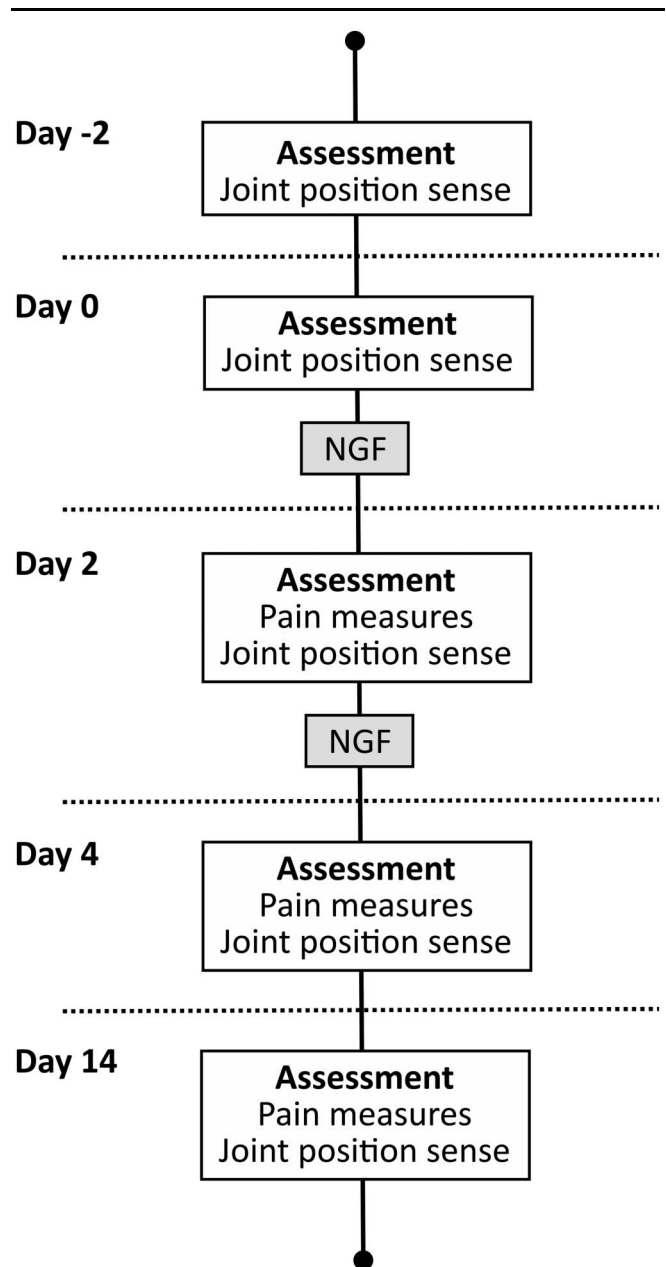


Figure 1. Experimental protocol. Participants attended 5 experimental sessions (days -2 , 0, 2, 4, and 14). Nerve growth factor (NGF) was administered on days 0 and 2. Wrist joint position sense (JPS) was recorded on each day. Pain measures (pain intensity, body chart pain drawings, and pain descriptors using the short-form McGill pain questionnaire) and mechanical hyperalgesia (pressure pain thresholds [PPTs]) were recorded on days 0, 2, 4, and 14.

lateral to a point that was 5 cm distal to the lateral epicondyle.⁹ Palpation of the muscle belly of ECRB during resisted wrist extension and radial deviation confirmed the injection site. A mark was drawn around the injection site with a permanent marker to ensure consistent placement of the injection in ECRB across sessions.

2.4. Pain assessment

An 11-point NRS was used to assess pain intensity of the injected arm with 0 = no pain and 10 = worst pain imaginable. To identify the location of pain, participants were asked to draw a line around the painful area on an anatomical picture of the upper limb.^{2,9} The

painful area of the upper limb was represented as the total area marked on the anterior and posterior surfaces of the upper arm.^{9,21,42} The short-form McGill pain questionnaire was used to indicate the quality of experimental pain.³⁰

2.5. Mechanical hyperalgesia

Pressure pain thresholds were measured with an electronic algometer (Algometer Type II; Somedic AB, Sollentuna, Sweden) applied to 4 sites: (1) right ECRB (injection site) muscle, (2) left ECRB muscle, (3) right tibialis anterior muscle, and (4) left tibialis anterior muscle. Site 1 and 2 were located as described in the NGF injection section, whereas the tibialis anterior sites were identified as one-third of the distance from the inferior border of the patella to the midpoint of the transverse crease of the ankle and 2.5 cm lateral to the tibial tuberosity.²¹ Pressure was applied through the algometer (1 cm² probe) and increased at a rate of 30 kPa/second perpendicular to the surface of the skin. Participants were requested to say “stop” when the pressure sensation first became painful and the pressure was recorded. All sites were assessed 3 times at 1-minute intervals, and the average PPT of the 3 measurements was used for statistical analysis.

2.6. Recording wrist joint position sense

Participants were seated in an upright position with the right forearm resting on a horizontal platform in midposition between pronation and supination with the elbow in approximately 90° flexion.⁴⁷ The forearm was stabilized using an adjustable brace at the elbow and an adjustable clamp proximal to the wrist (**Fig. 2A**). This setup ensured that participants started in the same position across experimental sessions, allowed unconstrained wrist motion and forearm rotation, and prevented upper limb movements from affecting performance of the radial/ulnar repositioning task. As the ECRB muscle acts as an agonist during radial deviation and an antagonist during ulnar deviation,⁴⁵ it was anticipated that injection of NGF into ECRB would disrupt position sense assessed through ulnar and radial deviation.

In the first experimental session (day -2), the neutral position of the wrist, and maximal range of motion for radial and ulnar deviation were recorded. The neutral position was measured using a handheld goniometer, while maximal radial and ulnar ranges of motion were recorded using a laser pointer and a paper board. A small foam block with 2 laser pointers was attached to

the hand of each participant (**Fig. 2A**). Once the neutral position of the wrist was set, a blank paper board was placed 60 cm in front of the hand, and the position of the active laser on the paper board was marked corresponding to the “neutral position.” To identify maximal radial and ulnar range of motion, the position of the active laser on the paper board was marked in maximal radial and ulnar deviation. Two target regions were then drawn on the paper board: (1) 80% to 100% of maximal radial deviation range and (2) 20% to 40% of maximal ulnar deviation range⁸ (**Fig. 2B**). In addition to the active laser, the position of the reference laser was marked to ensure consistent orientation of the hand in the neutral position at the beginning of every experimental session (**Fig. 2B**). The paper board set for each participant was used across sessions to ensure reliable assessment of the experimental trials.

A 2-segment model was used to 3D model the right forearm and hand⁴¹ to allow for assessment of wrist joint position.²⁰ Six active markers were positioned over the segments, including 1 cluster of 3 reflective markers attached to the hand, and another cluster of 3 reflective markers attached to the forearm (**Fig. 2A**). Six virtual markers were digitised to identify the medial and lateral epicondyle, ulna and radial styloid, and head of the second and fifth metacarpal bones. Another virtual marker was set at the neutral position on the paper board to reflect the position of the active laser (or the “virtual laser pointer”). The virtual markers were used to create a 3D model of the forearm (medial and lateral epicondyle, ulna and radial styloid), hand (ulna and radial styloid, head of the second and fifth metacarpal bones), and virtual laser pointer (head of the second and fifth metacarpal bones, and position of the virtual marker). Movements of the clusters were recorded by one position sensor containing a 3 camera Optotrak Certus System (Northern Digital, Inc, Waterloo, Canada) at 200 Hz and processed using Visual 3D (C-Motion, Version 4; C-Motion, Germantown, MD). A video camera (Panasonic HC-V250, Osaka, Japan; sampling rate 80 Hz) was placed behind the paper board and used to record the active laser during the experimental trial. Video data of the active laser were extracted using MATLAB R2016b (Mathworks, Natick, MA) and correlated with the positioning data of the virtual laser to determine if one accurately reflected the other.

2.7. Experimental procedure for assessing wrist joint position sense

Each participant was blindfolded during the experiment. The investigator placed the participant’s wrist into a neutral position

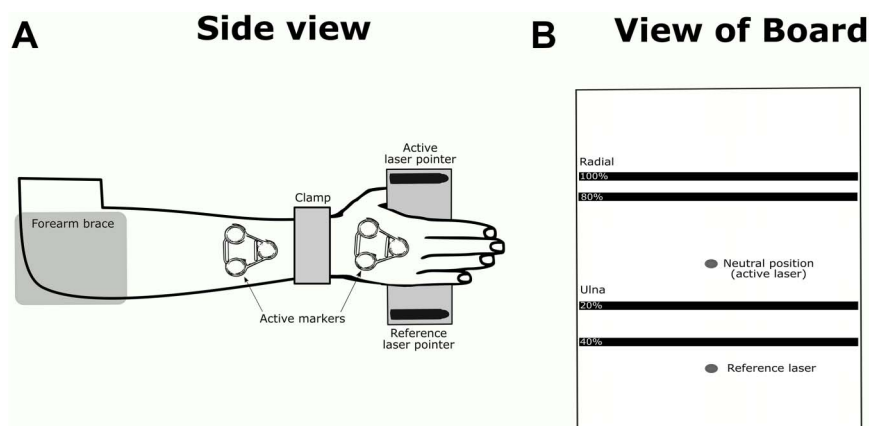


Figure 2. Experimental set-up for radial/ulnar reposition task that is showing the position of the upper arm from the side view (A) and the view of board (B) that is positioned in front of each participant.

by matching the active and reference lasers to their corresponding positions on the paper board (**Fig. 2B**). Participants were instructed to hold the hand in this position for 3 seconds and concentrate on “sensing” the hand position.^{7,32} They were then asked to deviate their hand towards either the radial or ulnar target zones. During radial deviation, the participants were instructed to stop once the investigator identified that they had reached the target zone (between 80% and 100% of radial deviation) marked on the paper board (**Fig. 2B**). The same protocol was applied when the participant moved their wrist in the ulnar direction (ulnar target zone = 20%–40% of maximal ulnar deviation) (**Fig. 2B**). After the participants reached the target zone, they were asked to return to the starting position (or the target position) as accurately as possible. This protocol was repeated 3 times in succession for both radial and ulnar deviation. Three movements to the radial target were always performed before movements to the ulnar target. Before the recorded trials, participants were allowed to practice the protocol once. The speed at which participants moved during the task was not controlled, and no feedback was given during testing. Participants were asked after every trial if they felt pain in the forearm during the repositioning task.

2.8. Data analysis

To calculate wrist JPS, the position of the virtual laser pointer in 2 target planes (medial-lateral and cephalic-caudal) was extracted from each trial using MATLAB R2016b (Mathworks). Movements in the medial-lateral direction were generated by wrist flexion-extension, while movements in the cephalic-caudal direction were generated by motions in the radial-ulnar deviation direction. A comparison between the virtual laser and the active laser demonstrated that these variables were highly correlated ($r > 0.97$), thus the coordinates of the virtual laser accurately reflected the position of the active laser and was used to calculate repositioning error (RE). Repositioning error was calculated as the mean distance between the target position (wrist neutral) and the participants attempt to match the target position following radial or ulnar deviation movements in all 3 trials. Repositioning error for the laser was expressed as (1) absolute error and (2) relative error.^{6,7} Absolute error reflected RE irrespective of error direction. This was calculated with Pythagoras theorem, using the virtual laser start position (wrist neutral) and the position of the virtual laser when participants attempted to reposition the wrist back to the start position (defined as “absolute error laser”). Relative error represented error in a particular direction and was calculated as the mean RE in the medial-lateral target plane and the cephalic-caudal target plane for all 3 trials for each target direction (defined as “relative error laser”). Wrist joint position in radial-ulnar deviation, pronation-supination, and flexion-extension were also extracted and used to calculate RE. Similar to above, RE for joint angles were calculated as the mean change in each of the 3 angles between the target position (wrist neutral), and the participants attempt to match the target position following radial and ulnar deviation movements in all 3 trials (defined as “joint-angle error”). In addition, the average velocity of the virtual laser for all 3 movements in the radial and ulnar direction was extracted (using visual 3D software) and used for the analysis of movement speed.

2.9. Statistical analysis

Statistical Package for the Social Sciences (SPSS) software (version 23 IBM Corp, Armonk, NY) was used for statistical analysis. All data were assessed for normality using visual

inspection (Q-Q plot) and Shapiro–Wilk test. Intraclass correlation coefficients (ICCs, 2-way mixed effects) were performed on absolute, relative, and joint-angle REs across days –2 and 0. The ICC values were interpreted based on the following criteria: poor (<0.50), moderate (0.50–0.65), good (0.65–0.80), or excellent (>0.80).³⁶ Pressure pain thresholds, velocity of the virtual laser, and RE (absolute, relative, and joint angle) data were compared between days 0, 2, 4, and 14 using 1-way repeated-measures analysis of variance (ANOVA). Data that did not meet assumptions of normality were positive skewed and log or square root transformed. Where appropriate, post hoc analyses were performed using the Holm–Sidak method corrected for multiple comparisons, and the Greenhouse–Geisser correction was applied if data did not meet the assumption of sphericity. Because of the lack variance in the data at day 0 (all scores were zero), pain intensity (NRS scores) were compared between days 0, 2, 4, and 14 using the Friedman test, and if significant, post hoc comparisons were performed using the Wilcoxon signed-rank test. Effect sizes were reported as eta-squared for absolute, relative, and joint-angle REs. Statistical significance was set at $P < 0.05$.

3. Results

3.1. Assessment of test–retest reliability

The results demonstrated good to excellent test–retest reliability of the JPS method in the absence of pain (day –2 vs day 0), with ICC values ranging from 0.66 to 0.89 for absolute, relative, and joint-angle REs following both radial and ulnar deviation movements (**Table 1**).

3.2. Nerve growth factor–induced pain

On day 0 and 2, NGF was injected after the assessment of PPTs and wrist JPS. Three individuals did not develop pain in response to NGF injection and were excluded from analyses (mean \pm SD, 22 ± 2 years; 1 female). For the remaining 25 participants, NGF-induced pain was local to the injection site and spread distal to the lower forearm and hand at days 2 and 4 (**Fig. 3**). Five participants reported an ache that radiated to the upper arm (towards the axilla) at days 2 and 4, that was not present on day 14. On the McGill Pain Questionnaire, NGF-induced muscle pain was commonly described as aching (87% of participants), tender (83%), and/or cramping (41%) at day 2. Similar descriptions were given on day 4—aching (80%), throbbing (32%), cramping (41%), and tender (80%). Numerical rating scores corresponding to NGF-induced pain (Friedman: $\chi^2(3) = 67.10$, $P < 0.001$) increased at day 2 (mean [SE] at day 2, $3.23 [0.41]$; post hoc: day 0 vs day 2: $P < 0.001$), remained elevated at day 4 (mean [SE] at day 4, $3.14 [0.38]$; post hoc: day 0 vs day 4: $P < 0.001$), and returned toward baseline values at day 14 (mean [SE] at day 14, $0.32 [0.13]$; post hoc: day 0 vs day 14: $P = 0.13$). No pain was reported in the forearm during the assessment of wrist JPS.

3.3. Mechanical hyperalgesia

Pressure pain thresholds over the right (injected) ECRB muscle reduced (ANOVA: $F_{3, 72} = 36.7$, $P < 0.001$) at day 2 and 4 compared with day 0 (both: $P < 0.001$) and returned toward baseline values at day 14 (post hoc: day 0 vs day 14: $P = 0.39$) (**Fig. 4**). There was no change in PPTs over the left ECRB muscle (ANOVA: $F_{3, 72} = 2.7$, $P = 0.05$) or over the left (ANOVA: $F_{3, 72} = 1.9$, $P = 0.12$) and right (ANOVA: $F_{3, 72} = 2.5$, $P = 0.06$) tibialis anterior muscles.

Table 1

Test-retest reliability for the assessment of wrist joint position sense between days –2 and 0.

	ICC	95% CI	P
Reposition error (radial)			
Absolute error laser	0.74	0.45–0.89	<0.001
Relative error laser (medial-lateral)	0.76	0.42–0.90	0.001
Relative error laser (cephalic-caudal)	0.89	0.73–0.95	<0.001
Joint-angle error (radial-ulnar deviation)	0.81	0.57–0.92	<0.001
Joint-angle error (pronation-supination)	0.78	0.50–0.91	<0.001
Joint-angle error (flexion-extension)	0.72	0.32–0.89	0.003
Reposition error (ulnar)			
Absolute error laser	0.87	0.70–0.95	<0.001
Relative error laser (medial-lateral)	0.79	0.52–0.92	<0.001
Relative error laser (cephalic-caudal)	0.79	0.50–0.91	<0.001
Joint-angle error (radial-ulnar deviation)	0.66	0.20–0.86	0.007
Joint-angle error (pronation-supination)	0.89	0.74–0.95	<0.001
Joint-angle error (flexion-extension)	0.64	0.19–0.85	0.007

CI, confidence interval; ICC, intraclass correlation coefficient.

3.4. Influence of sustained muscle pain on wrist joint position sense

Measures of absolute, relative, and joint-angle error were not altered by sustained muscle pain across days 0, 2, 4, and 14 (Table 2). However, there was a trend for a difference in absolute and joint-angle errors across days following ulnar deviation (Table 2). The speed at which participants moved was unchanged across experimental sessions in both the radial (ANOVA: $F_{3, 69} = 1.1$, $P = 0.36$) and ulnar (ANOVA: $F_{3, 72} = 1.7$, $P = 0.18$) directions.

4. Discussion

This study examined JPS in the transition to sustained musculoskeletal pain using a clinically relevant experimental pain model that elicited muscle pain and mechanical hyperalgesia similar to those symptoms associated with persistent pain.²¹ Contrary to the study hypothesis, the data demonstrated no statistical change in wrist joint position error in response to sustained lateral elbow pain. These data suggest that pain and hyperalgesia over 4 days does not impact the ability to sense a position of a limb in space and does not seem to produce the deficits in JPS observed in persistent pain populations or in the presence of experimentally induced DOMS.

Numerous studies have demonstrated impaired JPS in persistent musculoskeletal pain conditions,^{4,5,7,32,46} but when

these impairments in position sense develop in the transition from initial to sustained pain is not known. This study is the first to characterise JPS as pain develops and is sustained over 4 days, with resolution after 14 days. Interestingly, this study demonstrates that prolonged pain and hyperalgesia over 4 days does not impact JPS. This finding is consistent with previous studies that have assessed JPS during acute experimental pain induced by injection of hypertonic saline (with pain lasting a maximum of 15 minutes).^{6,29,44} However, the results contrast with studies using DOMS, which demonstrate deficits in JPS in the presence of pain and muscle damage for up to 3 days.^{11,34,35,41,51} This discrepancy is likely explained by the presence of muscle damage in the DOMS model. Indeed, muscle damage induced by eccentric exercise has been hypothesised to extend to the intrafusal fibres of muscle spindles, producing a fall in the spindle discharge rate, as well as altering resting tension in the muscle, leading to reduced spindle output at set muscle lengths.^{11,35,41,51} However, in none of these studies were the firing rates of muscle spindles recorded. As awareness of limb position is derived from peripheral inputs, change to muscle spindle activity is a likely mechanism for impaired JPS in DOMS where muscle damage occurs.^{37,39} Although DOMS is a useful model for investigating JPS in acute pain, there are clear differences between this model and NGF. Unlike DOMS, an NGF model allows for the investigation of understanding changes in JPS with pain in the absence of tissue damage, which more closely mimics a persistent pain model. In a clinical population, persistent pain may exist despite no observable pathological changes to tissues.¹⁴ The present findings suggest that pain and hyperalgesia in the absence of tissue damage over 4 consecutive days is not sufficient to alter JPS.

Position sense involves both peripheral and central mechanisms.²⁸ In the periphery, proprioceptive information is supplied by mechanoreceptors in muscles, joints, and skin.³⁹ Muscle spindles are considered the main mechanoreceptor that provides information on position and movement sense, with some cutaneous receptors providing additional information.^{37,39} Proprioceptive signals from these receptors combine with central mechanisms (ie, body representations that provide information about the size and shape of the body segment) to inform the perception of where the body part is in space.^{27,28} One possibility is that a 4-day period of pain may not have been sufficient to alter peripheral and central mechanisms involved in JPS. Indeed, muscle spindle afferents in healthy human subjects during stimulation of group III and IV afferents, via injection of hypertonic saline, have been demonstrated to not alter fusimotor excitability

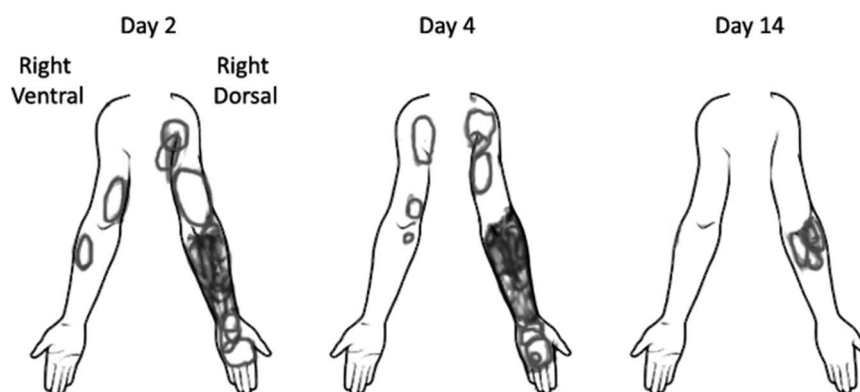


Figure 3. Body chart pain drawings showing distribution of pain in response to NGF administration at days 2, 4, and 14 for the 25 subjects. NGF, nerve growth factor.

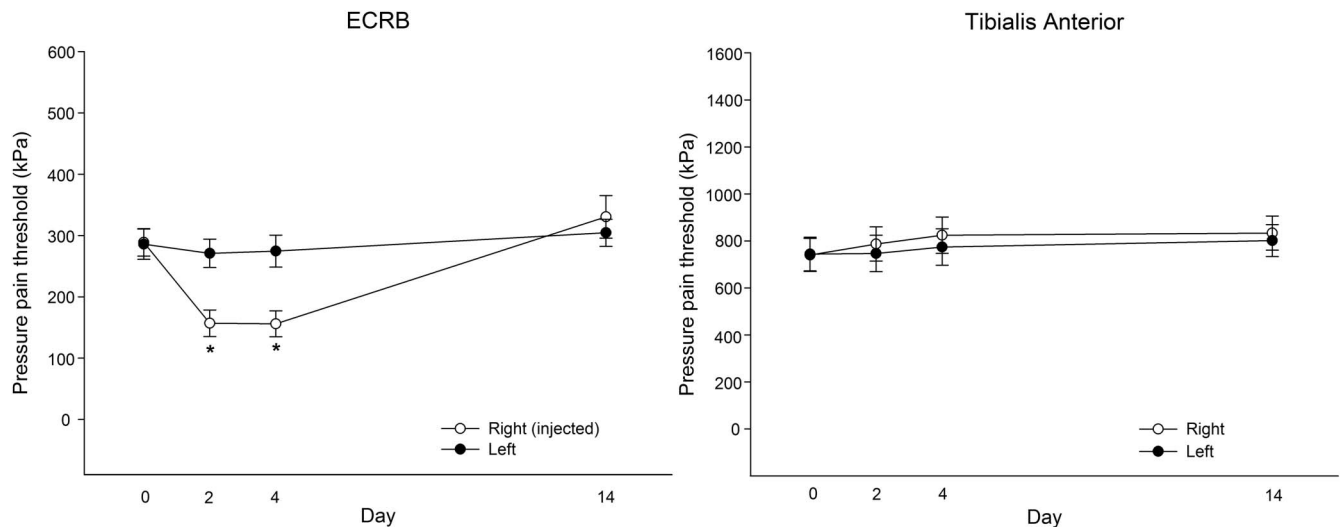


Figure 4. Group data (mean \pm SE, N = 25) for bilateral PPTs at the ECRB and tibialis anterior muscles at each time-point (days 0, 2, 4, and 14). * $P < 0.05$ relative to day 0. ECRB, extensor carpi radialis brevis; PPTs, pressure pain thresholds.

or muscle spindle discharge,^{10,18} with similar findings observed after a single injection of NGF.⁴⁹ However, in that NGF study, spindle firing was not directly recorded. Similarly, studies investigating the integrity of higher-order body representations during acute experimental pain suggest that acute nociceptive input is not sufficient to disrupt the working body schema.^{25,31} Together, these findings suggest that peripheral and central mechanisms that derive our awareness of position sense are intact during acute experimental pain and remain unchanged in the first 4 days of a pain experience.^{6,29,44} It is possible that a longer duration of pain (beyond a 4-day period) may be required to interfere with proprioceptive function.¹⁸ To some degree, this is supported by a trend for an increase in absolute and joint-angle error across days 2, 4, and 14 compared with baseline following ulnar deviation, suggesting that altered JPS may have occurred if follow-up measures were taken beyond day 4 (eg, 5–10 days after NGF where pain is still likely to be present^{24,25}).

Another possible explanation could be that unlike experimental pain, persistent pain is commonly associated with an array of psychosocial features.¹⁶ For example, fear avoidance and

functional disability have been associated with impaired JPS in people with persistent low back pain.³² Thus, features other than pain alone may explain why deficits in JPS are observed in persistent pain conditions and not in a healthy individual induced with short-term experimental pain. Future research is required to disentangle the inputs that contribute to deficits in JPS in persistent musculoskeletal pain conditions, as well as determine where, in the transition to persistent pain, impairments in JPS develop.

It should also be noted that JPS is one component of proprioception, and this study cannot exclude an effect of sustained pain on other components such as movement sense or force sense. Indeed, some studies have found that acute muscle pain induced by injection of hypertonic saline did not affect JPS but did affect movement detection threshold.^{29,44} Similarly, Weerakkody et al.⁵³ demonstrated that force sense at the elbow joint was impaired by acute muscle pain induced at the biceps. However, whether sustained muscle pain affects movement or force sense is not known and requires further investigation.

Table 2

Repositioning error results (mean \pm SD).

	Day 0	Day 2	Day 4	Day 14	F-value	df: error	P	Eta-squared
Reposition error (radial)								
Absolute error laser	1.7 \pm 0.9	1.8 \pm 1.1	1.9 \pm 0.9	1.9 \pm 1.1	0.44	3:69	0.72	1.7
Relative error laser (medial-lateral)	0.7 \pm 0.5	0.7 \pm 0.9	0.9 \pm 0.5	0.8 \pm 0.6	0.66	3:69	0.57	2.8
Relative error laser (cephalic-caudal)	1.4 \pm 0.9	1.6 \pm 1.1	1.5 \pm 0.9	1.7 \pm 1.2	0.43	3:69	0.74	1.8
Joint-angle error (radial-ulnar deviation)	2.4 \pm 2.0	2.6 \pm 2.6	2.3 \pm 1.7	2.3 \pm 2.1	0.19	3:69	0.90	0.8
Joint-angle error (pronation-supination)	0.7 \pm 0.5	0.6 \pm 0.4	0.7 \pm 0.5	0.6 \pm 0.5	0.92	3:69	0.43	3.9
Joint-angle error (flexion-extension)	1.8 \pm 1.5	1.5 \pm 1.4	1.6 \pm 1.2	1.6 \pm 1.2	0.33	3:69	0.80	1.4
Reposition error (ulnar)								
Absolute error laser	1.5 \pm 0.9	1.7 \pm 1.0	1.8 \pm 1.3	2.0 \pm 1.0	2.68	3:66	0.05	10.9
Relative error laser (medial-lateral)	0.6 \pm 0.3	0.5 \pm 0.3	0.6 \pm 0.6	0.7 \pm 0.5	0.66	2:45*	0.52	2.9
Relative error laser (cephalic-caudal)	1.0 \pm 1.2	1.3 \pm 1.4	1.2 \pm 1.5	1.6 \pm 1.3	1.80	3:66	0.15	7.6
Joint-angle error (radial-ulnar deviation)	1.6 \pm 1.2	2.1 \pm 1.5	2.1 \pm 1.7	2.4 \pm 1.7	2.42	3:66	0.07	9.9
Joint-angle error (pronation-supination)	0.6 \pm 0.5	0.7 \pm 0.9	0.5 \pm 0.4	0.8 \pm 0.6	1.64	3:66	0.19	6.9
Joint-angle error (flexion-extension)	1.2 \pm 0.8	1.0 \pm 0.9	1.2 \pm 1.1	1.3 \pm 1.0	1.57	3:66	0.21	6.7

P-values, F-values, and degrees of freedom (df) are from the primary repeated-measures ANOVA; absolute and relative repositioning errors are represented in centimetres; Joint-angle errors are represented in degrees; eta-squared values are represented as percentages.

* Greenhouse–Geisser correction applied.

ANOVA, analysis of variance.

This study used a reliable assessment of wrist JPS. The method demonstrated good to excellent test–retest reliability, which is similar to other repositioning tasks conducted on the wrist,^{50,51} neck,⁶ back,¹⁰ and knee.² Thus, it is unlikely that the null findings in this study are due to an unreliable measurement technique. Despite the rigorous approach, this study is not without limitations. A control group was not used, thus the time course of JPS in the absence of pain over 14 days is unknown. However, the assessment of JPS demonstrated excellent test–retest reliability across the first 2 pain-free days, suggesting stability of JPS over time. The method used to assess JPS did not account for thixotropic properties of the forearm muscles (ie, muscle spindle background activity) before the assessment of JPS, which may have introduced variability across each experimental trial.^{39,52} Thixotropy, however, is believed to be a property of passive muscle, with influence on proprioception during passive limb repositioning tasks, so it is likely to have had limited influence on active repositioning used in this study.³⁹ There is a possibility that participants may have gained feedback from the sensation of reaching maximal radial deviation that aided repositioning of the hand to wrist neutral. However, as ulnar deviation was prescribed between 20% and 40% of maximal range, participants may not have achieved the same end-range feedback as what may have been experienced through radial deviation, and this could have allowed more room for errors to occur during ulnar deviation. As a sample size calculation was not conducted, it is not known whether this study was powered to detect an effect of sustained pain on wrist JPS. However, given the exploratory nature of this investigation, there were no existing data on which to estimate a sample size.

Another consideration was that no participant reported pain during the assessment of JPS, and this may have contributed to the null findings. However, previous studies have shown no change in JPS even when pain severity is mild (3/10) to moderate (5/10) during the assessment.^{6,29,44} Thus, the unreported levels of pain when JPS was assessed may not be a major issue in this study. Given that an active repositioning task was performed, participants may have been using a sense of muscle effort during the task to assist repositioning accuracy. However, as participants were not asked about the strategy they used during the assessment, this cannot be determined in the current study. Furthermore, passive repositioning tasks are believed to provide more precise positional information than active repositioning tasks due to increased fusimotor activity during the voluntary contraction.^{1,3,55} Consequently, the active repositioning task used may have been less sensitive to detect changes in position sense in response to sustained pain than a passive repositioning task. Further research is required to test whether sustained pain affects JPS using a passive repositioning task. Finally, JPS was assessed on young adults (age, mean \pm SD 23 \pm 4 years), thus it is not known if these findings would be replicated in older populations. Given that impairments in JPS worsen with age,¹⁹ it is possible that baseline JPS may be more affected by pain in older subjects. Further research is required to test this possibility.

5. Conclusion

This study found no statistical change in wrist JPS after 4 days of sustained muscle pain at the elbow. These data suggest that pain and hyperalgesia sustained for 4 days does not impact the ability to sense a position of a limb in space and does not produce the same deficits in JPS observed in persistent pain populations or DOMS. Future research is required to disentangle the inputs that contribute to deficits in JPS in persistent musculoskeletal pain

conditions, as well as determine where, in the transition to persistent pain, impairments in JPS develop, so that effective treatments can be provided at a meaningful time-point.

Disclosures

The authors have no conflict of interest to declare.

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